

PATENT COOPERATION TREATY

AUG 10 2000

From the INTERNATIONAL SEARCHING AUTHORITY

To: JANE MASSEY LICATA LAW OFFICES OF JANE MASSEY LICATA 66 E. MAIN STREET MARLTON, NJ 08053	Docket System <input checked="" type="checkbox"/>
Status Report <input checked="" type="checkbox"/>	Docket Book <input checked="" type="checkbox"/>
101-1/00 AUS	

**PCT**

**NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL SEARCH REPORT  
OR THE DECLARATION**

(PCT Rule 44.1)

Applicant's or agent's file reference ISPH-0451	Date of Mailing (day/month/year) <b>07 AUG 2000</b>
International application No. PCT/US00/08794	International filing date (day/month/year) 04 April 2000 (04.04.2000)
Applicant ISIS PHARMACEUTICALS, INC.	

1.  The applicant is hereby notified that the international search report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompany sheet.

**Where?** Directly to the International Bureau of WIPO

34, chemin des Colombettes  
1211 Geneva 20, Switzerland  
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2.  The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3.  With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

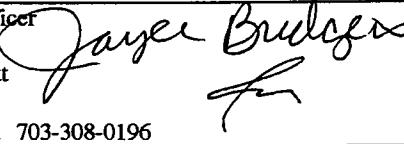
4. Further action(s): The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau.

If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer George Elliott  Telephone No. 703-308-0196
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# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference ISPH-0451	<b>FOR FURTHER ACTION</b>	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US00/08794	International filing date ( <i>day/month/year</i> ) 04 April 2000 (04.04.2000)	(Earliest) Priority Date ( <i>day/month/year</i> ) 06 April 1999 (06.04.1999)
Applicant ISIS PHARMACEUTICALS, INC.		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 3 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the Report**
  - a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
    - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
  - b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:
    - contained in the international application in written form.
    - filed together with the international application in computer readable form.
    - furnished subsequently to this Authority in written form.
    - furnished subsequently to this Authority in computer readable form.
    - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
    - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
2.  **Certain claims were found unsearchable (See Box I).**
3.  **Unity of invention is lacking (See Box II).**
4. With regard to the title,
  - the text is approved as submitted by the applicant.
  - the text has been established by this Authority to read as follows:
5. With regard to the abstract,
  - the text is approved as submitted by the applicant.
  - the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. The figure of the drawings to be published with the abstract is Figure No.
  - as suggested by the applicant.
  - because the applicant failed to suggest a figure.
  - because this figure better characterizes the invention.

None of the figures

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/08794

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07H 21/04, 21/02; C12Q 1/68; C12N 5/00; A01N 43/04; A61K 31/70  
 US CL : 536/23, 24.31, 24.33, 24.5; 435/6, 91, 31, 325, 375; 514/55

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.1, 24.31, 24.33, 24.5; 435/6, 91, 31, 325, 375; 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
 Please See Continuation Sheet

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	COHEN et al. The Critical Role of -38 MAP Kinase in T Cell HIV-1 Replication. Molecular Medicine. May 1997, Vol. 3, No. 5, pages 339-346, especially page 342.	19-22 and 31
Y		23-27
A	CROOKE, S.T. Basic Principles of Antisense Therapeutics. In: Antisense Research and Applications, Springer-Verlag Press, Berlin, Heidelberg, & New York. July 1998, pages 1-49, especially page 3.	1-40
A	BRANCH, A. A good antisense molecule is hard to find. TIBS. February 1998, Vol. 23, pages 45-50, especially page 45.	1-40

<input type="checkbox"/>	Further documents are listed in the continuation of Box C.	<input type="checkbox"/>	See patent family annex.
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* Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search	Date of mailing of the international search report
	07 AUG 2000

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer  George Elliott  Telephone No. 703-308-0196
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**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US00/08794

**Continuation of B. FIELDS SEARCHED Item3:** USPAT, EPO, JPO, DERWENT, DIALOG, CAplus  
Search terms: mitogen activated protein kinase, p38, inhibit, antagonist, antisense, aptamer, triplex, AS-OSN, oligonucleotide, ribozyme

## NOTES TO FORM PCT/ISA/220 (continued)

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:  
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:  
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:  
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or  
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:  
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

### "Statement under Article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

The statement should be brief, it should not exceed 500 words if in English or if translated into English.

It should not be confounded with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It should not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

### In what language ?

The amendments must be made in the language in which the international application is published. The letter and any statement accompanying the amendments must be in the same language as the international application if that language is English or French; otherwise, it must be in English or French, at the choice of the applicant.

### Consequence if a demand for international preliminary examination has already been filed ?

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

### Consequence with regard to translation of the international application for entry into the national phase ?

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.